THE AMERICAN JOURNAL OF HUMAN GENETICS

EDITOR
Charles J. Epstein, M.D.

ASSISTANT EDITOR
Shelley F. Diamond
University of California
San Francisco, California

ASSOCIATE EDITORS

David T. Bishop, Ph.D.
Imperial Cancer Research Fund
Leeds, England

Michael L. Boehnke, Ph.D.
University of Michigan
Ann Arbor, MI

John C. Carey, M.D.
University of Utah Medical Center
Salt Lake City, UT

Aravinda Chakravarti, Ph.D.
University of Pittsburgh
Pittsburgh, PA

Beverly S. Emanuel, Ph.D.
Children's Hospital of Philadelphia
Philadelphia, PA

William A. Gahl, M.D., Ph.D.
National Institute of Child Health and Human Development
Bethesda, MD

David H. Ledbetter, Ph.D.
Baylor College of Medicine
Houston, TX

Jurg Ott, Ph.D.
Columbia University
New York, NY

Neil J. Risch, Ph.D.
Yale University School of Medicine
New Haven, CT

Lap-Chee Tsui, Ph.D.
The Hospital for Sick Children
Toronto, Ontario

David Valle, M.D.
Johns Hopkins University School of Medicine
Baltimore, MD

John J. Wasmuth, Ph.D.
University of California
Irvine, CA

Huntington F. Willard, Ph.D.
Stanford University
Stanford, CA

Volume 48
1991

Published Monthly for
THE AMERICAN SOCIETY OF HUMAN GENETICS
BY THE UNIVERSITY OF CHICAGO PRESS

THE AMERICAN SOCIETY OF HUMAN GENETICS

BOARD OF DIRECTORS

President
Michael M. Kaback, M.D.
University of California
San Diego, CA

President-Elect
Walter E. Nance, M.D., Ph.D.
Medical College of Virginia
Richmond, VA

Secretary
Kenneth L. Garver, M.D., Ph.D.
Western Pennsylvania Hospital
Pittsburgh, PA

Treasurer
W. Allen Hogge, Ph.D.
University of Maryland
Baltimore, MD

Editor
Charles J. Epstein, M.D.
University of California
San Francisco, CA

President 1989
L. L. Cavalli-Sforza, M.D.
Stanford University
Stanford, CA

President 1990
C. Thomas Caskey, M.D.
Baylor College of Medicine
Houston, TX

Directors

Peter H. Byers, M.D.
University of Washington
Seattle, WA

Francis S. Collins, M.D., Ph.D.
University of Michigan Medical School
Ann Arbor, MI

David R. Cox, M.D.
University of California
San Francisco, CA

Beverly S. Emanuel, Ph.D.
Children's Hospital of Philadelphia
Philadelphia, PA

Laird G. Jackson, M.D.
Jefferson Medical College
Philadelphia, PA

Susan L. Naylor, Ph.D.
University of Texas Health Sciences Center
San Antonio, TX

Robert S. Sparkes, M.D.
University of California
Los Angeles, CA

David L. Valle, M.D.
Johns Hopkins University School of Medicine
Baltimore, MD

Ronald G. Worton, Ph.D.
Hospital for Sick Children
Toronto, Canada

© 1991 by The American Society of Human Genetics

Contents of Volume 48
January 1991

Original Articles

Mapping of Human Chromosome Xq28 by Two-Color Fluorescence In Situ Hybridization of DNA Sequences to Interphase Cell Nuclei
Barbara J. Trask, Hillary Massa, Sue Kenwrick, and Jane Gitschier 1

Chromosome 15 Uniparental Disomy Is Not Frequent in Angelman Syndrome
J. H. M. Knoll, K. A. Glatt, R. D. Nicholls, S. Malcolm, and M. Lalande 16

Allele Frequency Estimation from Data on Relatives
Michael Boehnke 22

A 3-bp Deletion in the Rhodopsin Gene in a Family with Autosomal Dominant Retinitis Pigmentosa
C. F. Inglehearn, R. Bashir, D. H. Lester, M. Jay, A. C. Bird, and S. S. Bhattacharya 26

Localization of the Åland Island Eye Disease Locus to the Pericentromeric Region of the X Chromosome by Linkage Analysis
Tiina Alitalo, Torben A. Kruse, Henrik Forsius, Aldur W. Eriksson, and Albert de la Chapelle 31

Pearson Syndrome and Mitochondrial Encephalomyopathy in a Patient with a Deletion of mtDNA
M. A. McShane, S. R. Hammans, M. Sweeney, I. J. Holt, T. J. Beattie, E. M. Brett, and A. E. Harding 39

Waardenburg Syndrome (WS): The Analysis of a Single Family with a WS1 Mutation Showing Linkage to RFLP Markers on Human Chromosome 2q
James H. Asher, Jr., Robert Morrell, and Thomas B. Friedman 43

Localization of DNA Sequences to a Region within Xp11.21 between Incontinentia Pigmenti (IP1) X-chromosomal Translocation Breakpoints
Jerome L. Gorski, Eric N. Burright, Catherine E. Harnden, Constance K. Stein, Thomas W. Glover, and Eric L. Reyner 53

Use of Short Sequence Repeat DNA Polymorphisms after PCR Amplification to Detect the Parental Origin of the Additional Chromosome 21 in Down Syndrome
Michael B. Petersen, Albert A. Schinzel, Franz Binkert, Lisbeth Tranebjaerg, Margareta Mikkelsen, Felicity A. Collins, Effrosini P. Economou, and Stylianos E. Antonarakis 65

Immunochemical Studies of Ferrochelatase Protein: Characterization of the Normal and Mutant Protein in Bovine and Human Protoporphyria
James G. Straka, Hazel D. Hill, Joan M. Krikava, Ann M. Kools, and Joseph R. Bloomer 72

Distribution of Deletions and Seven Point Mutations on CYP21B Genes in Three Clinical Forms of Steroid 21-Hydroxylase Deficiency
Etienne Mornet, Patrice Crété, Frédérique Kuttenn, Marie-Charles Raux-Demay, Joelle Boué, Perrin C. White, and André Boué 79

Mucopolysaccharidosis Type VII: Characterization of Mutations and Molecular Heterogeneity
Shunji Tomatsu, Seiji Fukuda, Kazuko Sukegawa, Yuko Ikedo, Shinji Yamada, Yukiji Yamada, Toshiya Sasaki, Hiroyuki Okamoto, Takashi Kuwahara, Seiji Yamaguchi, Tadashi Kiman, Haruo Shintaku, Gen Isshiki, and Tadao Orii 89

Analysis of the Chondroitin Sulfate Proteoglycan Core Protein (CSPGCP) Gene in Achondroplasia and Pseudoachondroplasia
J. E. Finkelstein, K. Doege, Y. Yamada, R. E. Pyeritz, J. M. Graham, Jr., J. B. Moeschler, R. M. Pauli, J. T. Hecht, and C. A. Francomano 97

A Mutant Allele Common to the Type I Adenine Phosphoribosyltransferase Deficiency in Japanese Subjects
Akio Mimori, Yuji Hidaka, Veda C. Wu, Susan A. Tarlé, Naoyuki Kamatani, William N. Kelley, and Thomas D. Pallela 103

Four Chromosomal Breakpoints and Four New Probes Mark Out a 10-cM Region Encompassing the Fragile-X Locus (FRAXA)
F. Rousseau, A. Vincent, S. Rivella, D. Heitz, C. Triboli, E. Maestrini, S. T. Warren, G. K. Suthers, P. Goodfellow, J. L. Mandel, D. Toniolo, and I. Oberle 108

Fitting Mixture Distributions to Phenylthiocarbamide (PTC) Sensitivity
P. N. Jones and G. J. McLachlan 117

Identification of a Highly Polymorphic Microsatellite VNTR within the Argininosuccinate Synthetase Locus: Exclusion of the Dystonia Gene on 9q32-34 as the Cause of Dopa-responsive Dystonia in a Large Kindred
David J. Kwiatkowski, Torbjoern G. Nygaard, Deborah E. Schuback, Scott Perman, Joel M. Trugman, Susan B. Bressman, Robert E. Burke, Mitchell F. Brin, Laurie Ozelius, Xandra O. Breakefield, Stanley Fahn, and Patricia L. Kramer 121

mtDNA Polymorphism in Two Communities of Jews
Y. Tikochinski, U. Ritte, S. R. Gross, E. M. Praeger, and A. C. Wilson 129

Analysis of the VNTR Locus D1S80 by PCR Followed by High-Resolution PAGE
Bruce Budowle, Ranajit Chakraborty, Alan W. Giusti, Arthur J. Eisenberg, and Robert C. Allen 137

Mothers' Postcounseling Beliefs about the Causes of Their Children's Genetic Disorders
Jon Weil 145

A Family Study of Gilles de la Tourette Syndrome
David L. Pauls, Cindy L. Raymond, John M. Stevenson, and James F. Leckman 154

On the Inheritance of Abdominal Aortic Aneurysm
Partha P. Majumder, Pamela L. St. Jean, Robert E. Ferrell, Marshall W. Webster, and David L. Steed 164

Book Reviews

Huntington Disease: A Disorder of Families. By Susan E. Folstein
Reviewed by Michael Hayden 171

Human Chromosomes: Manual of Basic Techniques. By Ram S. Verma and Arvind Babu
Reviewed by Stuart Schwartz 172

DNA Technology and Forensic Science. Edited by J. Ballantyne, C. Sensabaugh, and J. Witkowski
Reviewed by Ranajit Chakraborty 173

Back Door to Eugenics. By Troy Duster
Reviewed by Arno G. Motulsky 174

Intelligence and Giftedness: The Contributions of Heredity and Early Environment. By Miles D. Storfer
Reviewed by F. Vogel 175

Errata

176

Announcements

Employment and Fellowship Opportunities 177

February 1991

Editorial

Invited Editorial: Putting the Genetics Back into Cytogenetics
M. A. Ferguson-Smith 179

Original Articles

In Situ Hybridization to Cytogenetic Bands of Yeast Artificial Chromosomes Covering 50% of Human Xq24-Xq28 DNA
Vittorio Montanaro, Amelia Casamassimi, Michele D'Urso, Jae-Young Yoon, Wadiha Freije, David Schlessinger, Maximilian Muenke, Robert L. Nussbaum, Salvatore Saccone, Silvana Maugeri, Anna Maria Santoro, Salvatore Motta, and Giuliano Della Valle 183

Why Are Autism and the Fragile-X Syndrome Associated? Conceptual and Methodological Issues
Ira L. Cohen, Vicki Sudhalter, Al Pfadt, Edmund C. Jenkins, W. Ted Brown, and Peter M. Vietze 195

Rapid Detection of the A→G(8344) Mutation of mtDNA in Italian Families with Myoclonus Epilepsy and Ragged-Red Fibers (MERRF)
Massimo Zeviani, Patrizia Amati, Nereo Bresolin, Carlo Antozzi, Giovanni Piccolo, Antonio Toscano, and Stefano DiDonato 203

Improved Molecular Diagnostics for Ornithine Transcarbamylase Deficiency
Markus Grompe, C. Thomas Caskey, and Raymond G. Fenwick 212

A Dimorphic 4-bp Repeat in the Cystic Fibrosis Gene Is in Absolute Linkage Disequilibrium with the ΔF508 Mutation: Implications for Prenatal Diagnosis and Mutation Origin
Farid F. Chehab, John Johnson, Elaine Louie, Michel Goossens, Ernie Kawasaki, and Henry Erlich 223

Two Frameshift Mutations in the Cystic Fibrosis Gene
Michael C. Iannuzzi, Robert C. Stern, Francis S. Collins, Catherine Tom Hon, Noriko Hidaka, Theresa Strong, Lisa Becker, Mitchell L. Drumm, Marga B. White, Bernard Gerrard, and Michael Dean 227

Genetic Analysis of Breast Cancer in the Cancer and Steroid Hormone Study
Elizabeth B. Claus, Neil Risch, and W. Douglas Thompson 232

High-Resolution Linkage Mapping for Susceptibility Genes in Human Polygenic Disease: Insulin-dependent Diabetes Mellitus and Chromosome 11q
R. N. Hyer, C. Julier, J. D. Buckley, M. Trucco, J. Rotter, R. Spielman, A. Barnett, S. Bain, C. Boitard, I. Deschamps, J. A. Todd, J. I. Bell, and G. M. Lathrop 243

Isolation and Mapping of 62 New RFLP Markers on Human Chromosome 11
Takashi Tokino, Ei-ichi Takahashi, Masaki Mori, Akira Tanigami, Tom Glaser, J. W. Park, Carol Jones, Tada-aki Hori, and Yusuke Nakamura 258

Demonstration of the Genuine Iso-12p Character of the Standard Marker Chromosome of Testicular Germ Cell Tumors and Identification of Further Chromosome 12 Aberrations by Competitive In Situ Hybridization
R. F. Suijerbuijk, A. Y. van de Veen, J. van Echten, C. H. C. M. Buys, B. de Jong, J. W. Oosterhuis, D. A. Warburton, J. J. Cassiman, D. Schonk, and A. Geurts van Kessel 269

Association of Treacher Collins Syndrome and Translocation 6p21.31/16p13.11: Exclusion of the Locus from These Candidate Regions
M. J. Dixon, E. Haan, E. Baker, D. David, N. McKenzie, R. Williamson, J. Mulley, M. Farrall, and D. Callen 274

Progress in the Search for Genetic Linkage with Tourette Syndrome: An Exclusion Map Covering More than 50% of the Autosomal Genome
Andrew J. Pakstis, Peter Heutink, David L. Pauls, Roger Kurlan, Ben J. M. van de Wetering, James F. Leckman, Lodewijk A. Sandkuyl, Judith R. Kidd, Guido J. Breedveld, Carmela M. Castiglione, James Weber, Robert S. Sparkes, Donald J. Cohen, Kenneth K. Kidd, and Ben A. Oostra 281

Differentiation of Duchenne and Becker Muscular Dystrophy Phenotypes with Amino- and Carboxy-Terminal Antisera Specific for Dystrophin
Dennis E. Bulman, E. Gordon Murphy, Elizabeth E. Zubrzycka-Gaarn, Ronald G. Worton, and Peter N. Ray 295

A Mutation in the Proα2(I) Gene (COL1A2) for Type I Procollagen in Ehlers-Danlos Syndrome Type VII: Evidence Suggesting That Skipping of Exon 6 in RNA Splicing May Be a Common Cause of the Phenotype
Nagaswami S. Vasan, Helena Kuivaniemi, Bruce E. Vogel, Ronald R. Minor, Joyce A. M. Wootton, Gerard Tromp, Rosanna Weksberg, and Darwin J. Prockop 305

Homozygous Tyrosinase Gene Mutation in an American Black with Tyrosinase-negative (Type IA) Oculocutaneous Albinism
Richard A. Spritz, Kathleen M. Strunk, Chih-Lin Hsieh, Gurbax S. Sekhon, and Uta Francke 318

Saturating the Region of the Polycystic Kidney Disease Gene with *Not*I Linking Clones
Heinz Himmelbauer, Greg G. Germino, Isabella Ceccherini, Giovanni Romeo, Stephen T. Reeders, and Anna-Maria Frischauf 325

X-linked Sideroblastic Anemia and Ataxia: Linkage to Phosphoglycerate Kinase at Xq13
Wendy H. Raskind, Ellen Wijsman, Roberta A. Pagon, Timothy C. Cox, Michael J. Bawden, Brian K. May, and Thomas D. Bird 335

Molecular Genetic Basis of Maple Syrup Urine Disease in a Family with Two Defective Alleles for Branched Chain Acyltransferase and Localization of the Gene to Human Chromosome 1
W. Joseph Herring, Stuart Litwer, James L. Weber, and Dean J. Danner 342

The Glycine Cleavage System: Structure of a cDNA Encoding Human H-Protein, and Partial Characterization of Its Gene in Patients with Hyperglycinemias
Hirohisa Koyata and Koichi Hiraga 351

Identification of a Serum Protein Polymorphism via Two-dimensional Electrophoresis: Family and Population Studies in Two Genetically Isolated Groups: North American Hutterites and Australian Aborigines
H. Harrison, K. Miller, C. Ober, S. Refetoff, M. Dick, and S. Elias 362

Population Variation of Human mtDNA Control Region Sequences Detected by Enzymatic Amplification and Sequence-specific Oligonucleotide Probes
Mark Stoneking, Dennis Hedgecock, Russell G. Higuchi, Linda Vigilant, and Henry A. Erlich 370

No Severe Bottleneck during Human Evolution: Evidence from Two Apolipoprotein C-II Deficiency Alleles
Weijun Xiong, Wen-Hsiung Li, Israel Posner, Taku Yamamura, Akira Yamamoto, Antonio M. Gotto, Jr., and Lawrence Chan 383

Protection against Malaria Morbidity: Near-Fixation of the α-Thalassemia Gene in a Nepalese Population
G. Modiano, G. Morpurgo, L. Terrenato, A. Novelletto, A. Di Rienzo, B. Colombo, M. Purpura, M. Mariani, S. Santachiara-Benerecetti, A. Brega, K. A. Dixit, S. L. Shrestha, A. Lania, W. Wanachiwanawin, and L. Luzzatto 390

Genetic Population Structure of Italy. II. Physical and Cultural Barriers to Gene Flow
Guido Barbujani and Robert R. Sokal 398

Tay-Sachs Disease in Moroccan Jews: Deletion of a Phenylalanine in the α-Subunit of β-Hexosaminidase
Ruth Navon and Richard L. Proia 412

Letters to the Editor

Age at Menarche as a Fitness Trait: Further Considerations
T. Edward Reed 420

Age at Menarche and Fitness: Reply to Reed
N. G. Martin and S. A. Treloar 421

Heterozygotes and Homozygotes: Discrimination by Chemical Cleavage of Mismatch
Irma Dianzani, Susan M. Forrest, Clara Camaschella, Enrico Gottardi, and Richard G. H. Cotton 423

Uniparental Disomy and Gene Localization
Albert A. Schinzel 424

Book Reviews

Molecular Biology of Aging. Edited by Caleb E. Finch and Thomas E. Johnson
Reviewed by Samuel Goldstein 426

Detection of Cancer Predisposition: Laboratory Approaches. Edited by L. Spatz, A. D. Bloom, and N. W. Paul
Reviewed by Michael Swift 426

The Genetics of Mood Disorders.
By Ming T. Tsuang and Stephen V. Faraone
Reviewed by F. Vogel 427

Human Genetic Information: Science, Law, and Ethics. Edited by Derek Chadwick, Greg Bock, and Julie Whelen
Reviewed by John C. Fletcher 428

Announcements

Employment and Fellowship Opportunities; Courses; Meetings and Workshops 430

March 1991

Editorial

Invited Editorial: Prenatal Screening for Hemoglobinopathies
James E. Bowman 433

Original Articles

Prenatal Screening for Hemoglobinopathies. I. A Prospective Regional Trial
Peter T. Rowley, Starlene Loader, Carol J. Sutera, Margaret Walden, and Alyssa Kozyra 439

Prenatal Screening for Hemoglobinopathies. II. Evaluation of Counseling
Starlene Loader, Carol J. Sutera, Margaret Walden, Alyssa Kozyra, and Peter T. Rowley 447

Prenatal Screening for Hemoglobinopathies. III. Applicability of the Health Belief Model
Peter T. Rowley, Starlene Loader, Carol J. Sutera, Margaret Walden, and Alyssa Kozyra 452

Genetic Mapping of New DNA Probes at Xq27 Defines a Strategy for DNA Studies in the Fragile X Syndrome
G. K. Suthers, J. C. Mulley, M. A. Voelckel, N. Dahl, M. L. Väisänen, P. Steinbach, I. A. Glass, C. E. Schwartz, B. A. van Oost, S. N. Thibodeau, N. E. Haites, B. A. Oostra, R. Giné, M. Carballo, C. P. Morris, J. J. Hopwood, and G. R. Sutherland 460

Assignment of Emery-Dreifuss Muscular Dystrophy to the Distal Region of Xq28: The Results of a Collaborative Study
G. Giacomo Consalez, Nick S. T. Thomas, Carol L. Stayton, Samantha J. L. Knight, Mae Johnson, Linton C. Hopkins, Peter S. Harper, Louis J. Elsas, and Stephen T. Warren 468

Mapping of the Locus for X-linked Cardioskeletal Myopathy with Neutropenia and Abnormal Mitochondria (Barth Syndrome) to Xq28
P. A. Bolhuis, G. W. Hensels, T. J. M. Hulsebos, F. Baas, and P. G. Barth 481

Optic Atrophy in Leber Hereditary Optic Neuroretinopathy Is Probably Determined by an X-chromosomal Gene Closely Linked to DXS7
Johanna Vilkki, Jurg Ott, Marja-Liisa Savontaus, Pertti Aula, and Eeva K. Nikoskelainen 486

mtDNA Depletion with Variable Tissue Expression: A Novel Genetic Abnormality in Mitochondrial Diseases
Carlos T. Moraes, Sara Shanske, Hans-Jürgen Tritschler, June R. Aprille, Francesca Andreetta, Eduardo Bonilla, Eric A. Schon, and Salvatore DiMauro 492

Deficiency of Complex III of the Mitochondrial Respiratory Chain in a Patient with Facioscapulohumeral Disease
Deborah M. Slipetz, June R. Aprille, Paul R. Goodyer, and R. Rozen 502

Characterization of a Large Genomic Deletion Associated with a Polymorphic Block of Repeated Dinucleotides in the Type III Procollagen Gene (COL3A1) of a Patient with Ehlers-Danlos Syndrome Type IV
Brendan Lee, Marina D'Alessio, Henrik Vissing, Francesco Ramirez, Beat Steinmann, and Andrea Superti-Furga 511

Mild Spondyloepiphyseal Dysplasia (Namaqualand Type): Genetic Linkage to the Type II Collagen Gene (COL2A1)
Carron Sher, Rajkumar Ramesar, Robert Martell, Ian Learmonth, Petros Tsipouras, and Peter Beighton 518

Cloning and Expression of the cDNA Encoding Human Fumarylacetoacetate Hydrolase, the Enzyme Deficient in Hereditary Tyrosinemia: Assignment of the Gene to Chromosome 15
Daniel Phaneuf, Yves Labelle, Dominique Bérubé, Karen Arden, Webster Cavenee, Richard Gagné, and Robert M. Tanguay 525

Thermolabile Methylenetetrahydrofolate Reductase: An Inherited Risk Factor for Coronary Artery Disease
Soo-Sang Kang, Paul W. K. Wong, Armando Susmano, Judy Sora, Marija Norusis, and Neal Ruggie 536

Intermediate Hyperhomocysteinemia Resulting from Compound Heterozygosity of Methylenetetrahydrofolate Reductase Mutations
Soo-Sang Kang, Paul W. K. Wong, Hans-Georg Otto Bock, Allen Horwitz, and Art Grix 546

Diagnosis of Heterozygous States for Adenine Phosphoribosyltransferase Deficiency Based on Detection of In Vivo Somatic Mutants in Blood T Cells: Application to Screening of Heterozygotes
Masayuki Hakoda, Hisashi Yamanaka, Naoto Kamatani, and Naoyuki Kamatani 552

Linkage Analysis of Familial Alzheimer Disease, Using Chromosome 21 Markers
Gerard D. Schellenberg, Margaret A. Pericak-Vance, Ellen M. Wijsman, Deborah K. Moore, Perry C. Gaskell, Jr., Larry A. Yamaoka, Jacqueline L. Bebout, Leojean Anderson, Kathleen A. Welsh, Christopher M. Clark, George M. Martin, Allen D. Roses, and Thomas D. Bird 563

Clinical and Molecular Diagnosis of Miller-Dieker Syndrome
William B. Dobyns, Cynthia J. R. Curry, H. Eugene Hoyme, Laura Turlington, and David H. Ledbetter 584

Linkage Disequilibrium and Modification of Risk for Huntington Disease
Shelin Adam, Jane Theilmann, Ken Buetow, Amy Hedrick, Colin Collins, Bernhard Weber, Marlene Huggins, and Michael Hayden 595

Distribution of Three α-Chain β-Hexosaminidase A Mutations among Tay-Sachs Carriers
Eugene E. Grebner and Jerzy Tomczak 604

A Mutation in the Second Nucleotide Binding Fold of the Cystic Fibrosis Gene
Lucy Osborne, Richard Knight, George Santis, and Margaret Hodson 608

***Km* Typing with PCR: Application to Population Screening**
Janice H. Kurth, Anne M. Bowcock, Henry A. Erlich, Sara Nevo, and Luigi L. Cavalli-Sforza 613

Rapid Detection of CA Polymorphisms in Cloned DNA: Application to the 5′ Region of the Dystrophin Gene
C. A. Feener, F. M. Boyce, and L. M. Kunkel 621

Identification of a Novel Phenylketonuria (PKU) Mutation in the Chinese: Further Evidence for Multiple Origins of PKU in Asia
Tao Wang, Yoshiyuki Okano, Randy C. Eisensmith, Wilson H. Y. Lo, Shu-Zhen Huang, Yi-Tao Zeng, and Savio L. C. Woo 628

Screening for Mutations in the Phenylalanine Hydroxylase Gene from Italian Patients with Phenylketonuria by Using the Chemical Cleavage Method: A New Splice Mutation
I. Dianzani, S. M. Forrest, C. Camaschella, G. Saglio, A. Ponzone, and R. G. H. Cotton 631

Letters to the Editor

Biostatistics in Paternity Testing Using Genetic Systems with Linkage Disequilibrium
Wolfgang R. Mayr 636

Reply to Mayr
Henry A. Erlich, William Klitz, and Michael Luce 637

A Novel Approach to Establish Permanent Lymphoblastoid Cell Lines: Epstein-Barr Virus Transformation of Cryopreserved Lymphocytes
Leslie G. Louie and Mary-Claire King 637

Book Review

Transplacental Disorders. Edited by Ronald Bellisario and Gerald J. Mizejewski
Reviewed by James D. Goldberg 639

Announcements

American Board of Medical Genetics; Survey; Call for Patients; Conferences and Workshop 640

April 1991

Original Articles

Autosomal Dominant Deletions of the Mitochondrial Genome in a Case of Progressive Encephalomyopathy
Valérie Cormier, Agnès Rötig, Marc Tardieu, Michel Colonna, Jean-Marie Saudubray, and Arnold Munnich 643

Germ-Line Deletions of mtDNA in Mitochondrial Myopathy
J. Poulton, M. E. Deadman, S. Ramacharan, and R. M. Gardiner 649

Recurrence Risk of a New Dominant Mutation in Children of Unaffected Parents
Ellen M. Wijsman 654

Estimation of Allele Frequencies for VNTR Loci
B. Devlin, Neil Risch, and Kathryn Roeder 662

Alcohol and Aldehyde Dehydrogenase Genotypes and Alcoholism in Chinese Men
Holly Read Thomasson, Howard J. Edenberg, David W. Crabb, Xiao-Ling Mai, Ronald E. Jerome, Ting-Kai Li, Shiou-Ping Wang, Yu-Tsai Lin, Ru-Band Lu, and Shih-Jiun Yin 677

The Parental Origin of the Single X Chromosome in Turner Syndrome: Lack of Correlation with Parental Age or Clinical Phenotype
Archana Mathur, Lisa Stekol, Desmond Schatz, Noel K. MacLaren, Marilyn L. Scott, and Barbara Lippe 682

A Human Gene Homologous to the Formin Gene Residing at the Murine Limb Deformity Locus: Chromosomal Location and RFLPs
Richard L. Maas, Lisa I. Jepeal, Sandra L. Elfering, Randall F. Holcombe, Cynthia C. Morton, Roger L. Eddy, Mary G. Byers, Thomas B. Shows, and Philip Leder **687**

Human Elastin Gene: New Evidence for Localization to the Long Arm of Chromosome 7
Michael J. Fazio, Marie-Genevieve Mattei, Edith Passage, Mon-Li Chu, Donald Black, Ellen Solomon, Jeffrey M. Davidson, and Jouni Uitto **696**

A Murine Model for Type III Tyrosinemia: Lack of Immunologically Detectable 4-Hydroxyphenylpyruvic Acid Dioxygenase Enzyme Protein in a Novel Mouse Strain with Hypertyrosinemia
Fumio Endo, Hideki Katoh, Shigenori Yamamoto, and Ichiro Matsuda **704**

Analysis of N-Acetylgalactosamine-4-Sulfatase Protein and Kinetics in Mucopolysaccharidosis Type VI Patients
D. A. Brooks, P. A. G. McCourt, G. J. Gibson, L. J. Ashton, M. Shutter, and J. J. Hopwood **710**

Human *CYP1A1* Gene: Cosegregation of the Enzyme Inducibility Phenotype and an RFLP
Daniel D. Petersen, Cindy E. McKinney, Kiyoko Ikeya, Hana H. Smith, Allen E. Bale, O. Wesley McBride, and Daniel W. Nebert **720**

Twenty-seven Nonoverlapping Zinc Finger cDNAs from Human T Cells Map to Nine Different Chromosomes with Apparent Clustering
Kay Huebner, Teresa Druck, Carlo M. Croce, and Hans-Jürgen Thiesen **726**

Sequencing of the Variant Thyroxine-binding Globulin (TBG)–Quebec Reveals Two Nucleotide Substitutions
Richard Bertenshaw, Kyoko Takeda, and Samuel Refetoff **741**

Pulsed-Field Electrophoresis Screening for Immunoglobulin Heavy-Chain (IGHC) Multigene Deletions and Duplications
Andrea Bottaro, Umberto Cariota, Mario DeMarchi, and Angelo O. Carbonara **745**

Analysis of the Relationship of von Willebrand Disease (vWD) and Hereditary Hemorrhagic Telangiectasia and Identification of a Potential Type IIA vWD Mutation (Ile865 to Thr)
Michael C. Iannuzzi, Noriko Hidaka, Michael Boehnke, Mary E. Bruck, Wahid T. Hanna, Francis S. Collins, and David Ginsburg **757**

Linkage Analysis in Spinal Muscular Atrophy, by Six Closely Flanking Markers on Chromosome 5
P. Sheth, S. Abdelhak, M. F. Bachelot, P. Burlet, M. Masset, D. Hillaire, F. Clerget-Darpoux, J. Frézal, G. M. Lathrop, A. Munnich, and J. Melki **764**

Chromosomal Origin of Small Ring Marker Chromosomes in Man: Characterization by Molecular Genetics
D. F. Callen, H. J. Eyre, M. L. Ringenbergs, C. J. Freemantle, P. Woodroffe, and E. A. Haan **769**

A t(4;22) in a Meningioma Points to the Localization of a Putative Tumor-suppressor Gene
Ronald H. Lekanne Deprez, Nicole A. Groen, Nick A. van Biezen, Anne Hagmeijer, Ellen van Drunen, Jan W. Kroper, Cees J. J. Avezaat, Dirk Bootsma, and Ellen C. Zwarthoff **783**

Phenylketonuria in U.S. Blacks: Molecular Analysis of the Phenylalanine Hydroxylase Gene
Karen J. Hofman, Gary Steel, Haig H. Kazazian, and David Valle **791**

Exonic Point Mutations in NADH-cytochrome B5 Reductase Genes of Homozygotes for Hereditary Methemoglobinemia, Types I and III: Putative Mechanisms of Tissue-dependent Enzyme Deficiency
Takanori Katsube, Norihiro Sakamoto, Yasushi Kobayashi, Ritsuko Seki, Masami Hirano, Kiyoh Tanishima, Akio Tomoda, Eisuke Takazakura, Toshitsugu Yubisui, Masazumi Takeshita, Yoshiyuki Sakaki, and Yasuyuki Fukumaki **799**

The Spectrum of β-Thalassemia Mutations in Taiwan: Identification of a Novel Frameshift Mutation
Liang-In Lin, Kuo-Sin Lin, Kai-Hsin Lin, and Hsuan-Chen Chang **809**

Letters to the Editor

mtDNA Heteroplasmy in Leber Hereditary Optic Neuroretinopathy
Valérie Cormier, Agnès Rötig, Christian Geny, Pierre Cesaro, Jean-Louis Dufier, and Arnold Munnich **813**

Concurrence of Dominant Piebald Trait and Fragile X Syndrome
Brenda Finucane, Charles I. Scott, Jr., and Michael B. Kurtz **815**

Cystic Fibrosis Patients with Liver Disease Are Not Genetically Distinct
Maurizio Ferrari, Carla Colombo, Gianfranco Sebastio, Ornella Castiglione, Serena Quattrucci, Bruno Dallapiccola, Giambattista Leoni, Maurizio Zanda, Luca Romano, and Marcella Devoto **815**

Announcements

Employment and Fellowship Opportunities; Call for Patients; Conference **817**

May 1991

Editorial

Invited Editorial: Research on DNA Typing Catching Up with Courtroom Application
Eric S. Lander **819**

Original Articles

The Efficiency of Multilocus DNA Fingerprint Probes for Individualization and Establishment of Family Relationships, Determined from Extensive Casework
Alec J. Jeffreys, Michelle Turner, and Paul Debenham **824**

Fixed-Bin Analysis for Statistical Evaluation of Continuous Distributions of Allelic Data from VNTR Loci, for Use in Forensic Comparisons
B. Budowle, A. M. Giusti, J. S. Waye, F. S. Baechtel, R. M. Fourney, Dwight E. Adams, Lawrence A. Presley, Harold A. Deadman, and K. L. Monson **841**

Cytogenetic Analysis of Sperm from a Man Heterozygous for a Pericentric Inversion, inv (3) (p25q21)
Renee H. Martin **856**

Use of the Robust Sib-Pair Method to Screen for Single-Locus, Multiple-Locus, and Pleiotropic Effects: Application to Traits Related to Hypertension
Alexander F. Wilson, Robert C. Elston, Lieu D. Tran, and Roger M. Siervogel **862**

Atopic Disease and Immunoglobulin E in Twins Reared Apart and Together
Bruce Hanson, Matthew McGue, Beatrice Roitman-Johnson, Nancy L. Segal, Thomas J. Bouchard, Jr., and M. N. Blumenthal **873**

Allele-specific Hypermethylation of the Retinoblastoma Tumor-suppressor Gene
Toshiyuki Sakai, Junya Toguchida, Naoko Ohtani, David W. Yandell, Joyce M. Rapaport, and Thaddeus P. Dryja **880**

Structure of the Chromosomal Gene and cDNAs Coding for Lactase-Phlorizin Hydrolase in Humans with Adult-Type Hypolactasia or Persistence of Lactase
Werner Boll, Peter Wagner, and Ned Mantei **889**

Extended Haplotypes and Linkage Disequilibrium between 11 Markers at the APOA1-C3-A4 Gene Cluster on Chromosome 11
P. Benlian, C. Boileau, N. Loux, D. Pastier, J. Masliah, M. Coulon, M. Nigou, A. Ragab, J. Guimard, J. B. Ruidavets, C. Bonaïti-Pellié, J. C. Fruchart, P. Douste-Blazy, G. Bereziat, and C. Junien **903**

A Detailed Multipoint Map of Human Chromosome 4 Provides Evidence for Linkage Heterogeneity and Position-specific Recombination Rates
Kenneth H. Buetow, Rita Shiang, Ping Yang, Yusuke Nakamura, G. Mark Lathrop, Raymond White, John J. Wasmuth, Stephen Wood, Laura D. Berdahl, Nancy J. Leysens, Timothy M. Ritty, Molly E. Wise, and Jeffrey C. Murray **911**

Testing for Association between Disease and Linked Marker Loci: A Log-linear-Model Analysis
Laurence Tiret, Philippe Amouyel, Roger Rakotovao, François Cambien, and Pierre Ducimetière **926**

Leber Hereditary Optic Neuropathy: Involvement of the Mitochondrial ND1 Gene and Evidence for an Intragenic Suppressor Mutation
Neil Howell, I. Kubacka, M. Xu, and D. A. McCullough **935**

Deletion of the Entire Cytochrome P450 CYP2D6 Gene as a Cause of Impaired Drug Metabolism in Poor Metabolizers of the Debrisoquine/Sparteine Polymorphism
Andrea Gaedigk, Martin Blum, Roger Gaedigk, Michel Eichelbaum, and Urs A. Meyers **943**

Identification of 17 Independent Mutations Responsible for Human Hypoxanthine-Guanine Phosphoribosyltransferase (HPRT) Deficiency
Beverly L. Davidson, Susan A. Tarlé, Mary Van Antwerp, Dorothy A. Gibbs, Richard W. E. Watts, William N. Kelley, and Thomas D. Palella **951**

Evidence for the Segregation of a Major Gene in Human Susceptibility/Resistance to Infection by *Schistosoma mansoni*
Laurent Abel, Florence Demenais, Aluizio Prata, Antonio E. Souza, and Alain Dessein **959**

Identification of a Mutation in Arylsulfatase A Gene of a Patient with Adult-Type Metachromatic Leukodystrophy
Rui Kondo, Nobuaki Wakamatsu, Hiide Yoshino, Nobuyoshi Fukuhara, Tadashi Miyatake, and Shoji Tsuji **971**

Proline at Position 36: A New Transthyretin Mutation Associated with Familial Amyloidotic Polyneuropathy
Lee Anna Jones, James C. Skare, Jennifer A. Harding, Alan S. Cohen, Aubrey Milunsky, and Martha Skinner **979**

2,8-Dihydroxyadenine Lithiasis in a Japanese Patient Heterozygous at the Adenine Phosphoribosyltransferase Locus
A. Sahota, J. Chen, M. A. Behzadian, R. Ravindra, H. Takeuchi, P. J. Stambrook, and J. A. Tischfield **983**

Chromosomal Assignments of the Human Endothelin Family Genes: the Endothelin-1 Gene (EDN1) to 6p23-p24, the Endothelin-2 Gene (EDN2) to 1p34, and the Endothelin-3 Gene (EDN3) to 20q13.2-q13.3
Tadao Arinami, Mishiyo Ishikawa, Akihiro Inoue, Masashi Yanagisawa, Tomoh Masaki, Michihiro C. Yoshida, and Hideo Hamaguchi **990**

Evidence for WT1 as a Wilms Tumor (WT) Gene: Intragenic Germinal Deletion in Bilateral WT
Vicki Huff, Hiroshi Miwa, Daniel A. Haber, Katherine M. Call, David E. Housman, Louise C. Strong, and Grady F. Saunders **997**

Molecular Analyses of an Acidic Transthyretin Asn 90 Variant
Maria João Mascarenhas Saraiva, Maria do Rosário Almeida, Isabel Longo Alves, Paulo Moreira, MaryAnn Gawinowicz, Pedro Pinho Costa, Silke Rauh, Angelika Banhzoff, and Klaus Altland **1004**

American Society of Human Genetics: Committee Report and Statement

American Society of Human Genetics Social Issues Committee Report on Genetics and Adoption: Points to Consider 1009

American Society of Human Genetics Statement on Clinical Genetics and Freedom of Choice 1011

Letters to the Editor

Further Evidence for an Association between Genetic Variation in Transforming Growth Factor Alpha and Cleft Lip and Palate
Georgia Chenevix-Trench, Kathleen Jones, Adele Green, and Nicholas Martin 1012

Association of Pigmentary Anomalies with Chromosomal and Genetic Mosaicism and Chimerism
R. Happle 1013

Different Clinical Manifestations of Hyperphenylalaninemia in Three Siblings with Identical Phenylalanine Hydroxylase Genes
Deborah DiSilvestre, Richard Koch, and John Groffen 1014

Erratum

1017

Announcements

Employment and Fellowship Opportunities; ABMG Certification Exams; Call for Patients; Meeting, Course, and Workshop 1018

June 1991

Editorial

Invited Editorial: The Genetics of Alzheimer Disease—A Teasing Problem
Jonathan L. Haines 1021

Original Articles

Segregation Analysis Reveals Evidence of a Major Gene for Alzheimer Disease
Lindsay A. Farrer, Richard H. Myers, Linda Connor, L. Adrienne Cupples, and John H. Growdon 1026

Linkage Studies in Familial Alzheimer Disease: Evidence for Chromosome 19 Linkage
M. A. Pericak-Vance, J. L. Bebout, P. C. Gaskell, Jr., L. H. Yamaoka, W.-Y. Hung, M. J. Alberts, A. P. Walker, R. J. Bartlett, C. A. Haynes, K. A. Welsh, N. L. Earl, A. Heyman, C. M. Clark, and A. D. Roses 1034

Fragile X Syndrome: Diagnosis Using Highly Polymorphic Microsatellite Markers
Robert I. Richards, Yang Shen, Katherine Holman, Helen Kozman, Valentine J. Hyland, John C. Mulley, and Grant R. Sutherland 1051

A Note on Multiple Testing Procedures in Linkage Analysis
Neil Risch 1058

Possible Linkage of the Estrogen Receptor Gene to Breast Cancer in a Family with Late-Onset Disease
P. Zuppan, J. M. Hall, M. K. Lee, M. Ponglikitmongkol, and M.-C. King 1065

Uniparental Heterodisomy for Chromosome 14 in a Phenotypically Abnormal Familial Balanced 13/14 Robertsonian Translocation Carrier
Jin-Chen C. Wang, Merry B. Passage, Pauline H. Yen, Larry J. Shapiro, and T. K. Mohandas 1069

Heterogeneity in X-linked Recessive Charcot-Marie-Tooth Neuropathy
Victor V. Ionasescu, James Trofatter, Jonathan L. Haines, Anne M. Summers, Rebecca Ionasescu, and Charles Searby 1075

Genetic Risks for Children of Women with Myotonic Dystrophy
Manuela C. Koch, Tiemo Grimm, Helen G. Harley, and Peter S. Harper 1084

Genetic and Environmental Explanations for the Distribution of Sodium-Lithium Countertransport in Pedigrees from Rochester, MN
Timothy R. Rebbeck, Stephen T. Turner, Virginia V. Michels, and Patricia P. Moll 1092

Identification of RNA Splicing Errors Resulting in Human Ornithine Transcarbamylase Deficiency
Russ P. Carstens, Wayne A. Fenton, and Leon E. Rosenberg 1105

Single-Strand Conformation Polymorphism for Detection of Mutations and Base Substitutions in Phenylketonuria
Philippe Labrune, Dominique Melle, Françoise Rey, Monique Berthelon, Catherine Caillaud, Jean Rey, Arnold Munnich, and Stanislas Lyonnet 1115

Congenital Deficiency of a 20-kDa Subunit of Mitochondrial Complex I in Fibroblasts
Deborah M. Slipetz, Paul R. Goodyer, and Rima Rozen 1121

Screening for Non-DeltaF508 Mutations in Five Exons of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Gene in Italy
Marcella Devoto, Patrizia Ronchetto, Pascale Fanen, Juan José Telleria Orriols, Giovanni Romeo, Michel Goossens, Maurizio Ferrari, Carmelina Magnani, Manuela Seia, and Laura Cremonesi 1127

Localization of the Translocation Breakpoint in a Female with Menkes Syndrome to Xq13.2-q13.3 Proximal to PGK-1
Vera Verga, Bryan K. Hall, Shirong Wang, Susan Johnson, James V. Higgins, and Thomas W. Glover 1133

A Third Mutation at the CpG Dinucleotide of Codon 504 and a Silent Mutation at Codon 506 of the *HEX A* Gene
Barry H. Paw, Ladonna C. Wood, and Elizabeth F. Neufeld 1139

A New mtDNA Mutation Associated with Leber Hereditary Optic Neuroretinopathy
Kirsi Huoponen, Johanna Vilkki, Pertti Aula, Eeva K. Nikoskelainen, and Marja-Liisa Savontaus 1147

Characterization of the Molecular Basis of the α 1-Antitrypsin F Allele
Hiroshi Okayama, Mark Brantly, Mark Holmes, and Ronald G. Crystal 1154

Tyrosinase Gene Mutations Associated with Type IB ("Yellow") Oculocutaneous Albinism
Lutz B. Giebel, Ram K. Tripathi, Kathleen M. Strunk, Jon M. Hanifin, Charles E. Jackson, Richard A. King, and Richard A. Spritz 1159

Identification of a Splice-Site Mutation in the Human Growth Hormone–variant Gene
James N. MacLeod, Stephen A. Liebhaber, Margaret H. MacGillivray, and Nancy E. Cooke 1168

$^{G}\gamma$ and $^{A}\gamma$ Globin Genes Are Identical from −471 of the Promoter Midway through γIVSII in a Benin β^{s} Haplotype Associated with Elevated Fetal Hemoglobin
N. Mishima, E. C. Brinson, P. F. Milner, and J. G. Gilman 1175

A Novel Mutation in the Invariant AG of the Acceptor Splice Site of Intron 4 of the β-Hexosaminidase α-Subunit Gene in Two Unrelated American Black G_{M2}-Gangliosidosis (Tay-Sachs Disease) Patients
Emilie H. Mules, Carol E. Dowling, Michael B. Petersen, Haig H. Kazazian, Jr., and George H. Thomas 1181

A Single Base Mutation in Type I Procollagen (COL1A1) That Converts Glycine α1-541 to Aspartate in a Lethal Variant of Osteogenesis Imperfecta: Detection of the Mutation with a Carbodiimide Reaction of DNA Heteroduplexes and Direct Sequencing of Products of the PCR
Jiapiao Zhuang, Constantinos D. Constantinou, Arupa Ganguly, and Darwin J. Prockop 1186

Review Article

Review and Hypothesis: Alzheimer Disease and Down Syndrome—Chromosome 21 Nondisjunction May Underlie Both Disorders
Huntington Potter 1192

Letters to the Editor

Genetics and Public Health: Means, Ends, and Justices
Abby Lippman 1201

Reply to Lippman
George C. Cunningham 1202

Reply to Lippman
Jessica G. Davis 1203

Update on Maternal Serum Alpha-Fetoprotein Screening
Kenneth L. Garver 1203

Ethics of a Genetic Program for Myotonic Dystrophy
Claude M. Laberge 1204

Reply to Laberge
Marc De Braekeleer and Marcel J. Melançon 1206

Can a Susceptibility Locus for Schizophrenia Be Excluded from Chromosome 5q11-13?
C. I. Amos, M. Martinez, and S. J. Bale 1206

Reply to Amos et al.
Peter McGuffin, Mathew Sargent, Simon Tidmarsh, Gillian Hetti, Stephen Whatley, and R. M. Marchbanks 1208

Allelic Mutations of the Fourth Subunit of NADH Dehydrogenase Are Not Pathogenetically Important in 11778-negative Leber Hereditary Optic Neuropathy
Donald R. Johns 1209

Reply to Johns
Neil Howell and David McCullough 1211

Homozygous Nonsense Mutation Causing Cystic Fibrosis with Uniparental Disomy
Arthur L. Beaudet, Ronald G. Perciaccante, and Garry R. Cutting 1213

Allan-Herndon Syndrome—or X-linked Cerebral Palsy?
Sarah Bundey, L. A. Comley, and Andrew Blair 1214

Human Error in Forensic DNA Typing
Russell Higuchi 1215

Book Reviews

***Human Prenatal Diagnosis*, 2d ed.** Edited by Karen Filkins and Joseph Russo
Reviewed by Melissa H. Fries 1217

Schizophrenia Genesis: The Origins of Madness. By Irving I. Gottesman
Reviewed by F. Vogel 1218

Announcements

Employment and Fellowship Opportunities; Course; ASHG Electronic Bulletin Board Termination 1219

Author Index to Volume 48 1221

Subject Index to Volume 48 1227

Contents of Volume 48 1237